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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/382,816	08/25/99	ROBINSON	D 2149-107

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EXAMINER	
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ART UNIT	**PAPER NUMBER**
1645	7

DATE MAILED: 07/14/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/382,816	Robinson
Examiner	**Group Art Unit**
Robert A. Zeman	1645

☒ Responsive to communication(s) filed on *Aug 25, 1999*.

☐ This action is **FINAL.**

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

A shortened statutory period for response to this action is set to expire *3* month(s), or thirty days, whichever is longer, from the mailing date of this communication. Failure to respond within the period for response will cause the application to become abandoned. (35 U.S.C. § 133). Extensions of time may be obtained under the provisions of 37 CFR 1.136(a).

Disposition of Claims

☒ Claim(s) *1-25* is/are pending in the application.

Of the above, claim(s) _____ is/are withdrawn from consideration.

☐ Claim(s) _____ is/are allowed.

☒ Claim(s) *1-25* is/are rejected.

☐ Claim(s) _____ is/are objected to.

☐ Claims _____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The drawing(s) filed on _____ is/are objected to by the Examiner.

☐ The proposed drawing correction, filed on _____ is ☐approved ☐disapproved.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. § 119

☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number) _____.

☐ received in this national stage application from the International Bureau (PCT Rule 17.2(a)).

*Certified copies not received: _____.

☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

Attachment(s)

☒ Notice of References Cited, PTO-892

☒ Information Disclosure Statement(s), PTO-1449, Paper No(s). *6*

☐ Interview Summary, PTO-413

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Notice of Informal Patent Application, PTO-152

--- SEE OFFICE ACTION ON THE FOLLOWING PAGES ---

DETAILED ACTION

Continuing Data

This application is a Continuation of Application No. 08/719,367 now U.S. Patent No. 6,022,730, filed 9/25/96, which is a Continuation-In-Part , of Application No. 08/261,977, filed 6/17/94, now abandoned.

Claim Status

Claims 1-25 are pending in this application.

Information Disclosure Statement

The IDS filed 6/26/00, as Paper No. 6, has been received and made of record.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-25 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-14 of U.S. Patent No. 6,022,730. Although the conflicting

claims are not identical, they are not patentably distinct from each other because both are drawn to methods of producing (isolating) bacteria from retrovirally transformed human endothelial cells.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter or any new and useful improvement thereof, may obtain a patent therefore, subject to the conditions and requirements of this title.

Claims 1-25 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a credible asserted utility or a well established utility, as the disclosed invention is inoperative.

The claims are drawn to a method for producing a bacterium that contains a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene. The specification at page 9 indicates that the present invention provides a process for producing a bacteria containing at least one eukaryotic gene. The specification at page 9 further states that "the process of the present invention, sometimes called *de novo* speciation, can be divided into the following stages:

(I) culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene; and

(II) selecting and replicating at least one such bacterium."

Accordingly, the claims and the specification call for a method for producing a bacterium containing a eukaryotic and/or viral gene, which comprises culturing virally-infected eukaryotic cells under low oxygen conditions to produce a bacterium containing a eukaryotic and/or viral gene whereby neither the bacterium nor the bacterial genome is introduced. In addition, Barron's Law Dictionary 3rd Edition defines *"de*

novo" as "new, young, fresh; renewed, revived..." and Webster's II New Riverside Dictionary defines "speciation" as "the evolutionary process by which new species are formed." Therefore, Applicant is calling for the *de novo* "creation" of a new species and/or the "creation of a life form", i.e., the bacterium, from eukaryotes without the introduction of bacterial genes or the bacteria themselves. However, current knowledge of scientific principles maintains that prokaryotes and eukaryotes constitute separate and distinct life forms having many differences in structure and function. The most striking one pertains to the presence or absence of a nucleus. That the only recognized process in the art for the acquisition of new traits is mutation is well settled. Moreover, the process of the acquisition of new traits is a slow process which requires so many changes that more than anaerobic cultivation for a few hours or even a few years is necessary. To the best of scientific knowledge, the evolution of first one-celled and then many-celled eukaryotes from one-celled prokaryotes is believed to have taken several million years and not a few hours or days. Likewise, it appears that Applicant is calling for the "spontaneous" production of a new bacterium without the introduction of the bacteria or the bacterial genome. However, it should be remembered that the principles of spontaneous generation were effectively disproved by Louis Pasteur at the end of the last century in historical experiments. Therefore, the specification fails to show a clear correlation between culturing retrovirally infected animal cells in the amount of oxygen given and the "creation" (i.e., the production) of a new species of bacteria.

Claim Rejections - 35 USC § 112

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is

most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The invention appears to employ novel strains of Staphylococcus and Micrococcus. It's not clear if the written description is sufficiently repeatable to avoid the need for a deposit. Further it is unclear if the starting materials were readily available to the public at the time of the invention.

It appears that a deposit was made in this application as filed (page 8). However, it is not clear if the deposit meets all of the requirements of the criteria set forth in 37 CFR 1.801-1.809. Applicant or Applicant's representative may provide assurance of compliance with the requirements or 35 U.S.C. § 112, first paragraph.

If the deposit was made under the provisions of the Budapest Treaty, filing of an affidavit or declaration by applicants or assignees, or a statement by an attorney of record over his or her signature and registration number, stating that the deposit has been accepted by an International Depository Authority under the provisions of the Budapest Treaty, that all restrictions upon public access to the deposit will be irrevocably removed upon the grant of a patent on this application and that the deposit will be replaced if viable samples cannot be dispensed by the depository, is required. This requirement is necessary when a deposit is made under provisions of the Budapest Treaty as the Treaty leaves these specific matters to the discretion of each State. Amendment of the specification to recite the date of the deposit and the complete name and address of the depository, amendment of the claims to refer to the accession number, is required, in addition, claims reciting the deposited material must be amended to include the depository accession number of the deposited material.

Furthermore, unless the deposit was made at or before the time of filing, a declaration filed under 37 C.F.R. 1.132 is necessary to construct a chain of custody. The declaration, executed by a person in a position to know, should identify the deposited the bacteria by the depository accession number,

establish that the bacteria is the same as that described in the specification, and establish that the deposited bacteria were in applicants' possession at the time of filing.

Claims 1-25 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method for isolating a bacterium comprising culturing retrovirally transformed human capillary microvascular endothelial cells; subjecting said culture to an anaerobic culturing phase; exposing the culture to oxygen conditions corresponding to an atmosphere containing greater than about 2% v/v oxygen; subjecting said culture to an additional anaerobic culturing phase; subjecting said culture to an additional aerobic culturing phase; isolating a bacterium (either *Staphylococcus areus* ATCC 55589, *Staphylococcus capitis* ATCC 55590, *Staphylococcus hemolyticus* ATCC 55592, *Staphylococcus epidermidis* ATTC 55591 or *Micrococcus luteus* ATCC 55588), does not reasonably provide enablement for methods for **producing** a bacterium that contains a eukaryotic and/or viral gene comprising culturing virally-infected eukaryotic cells under low oxygen conditions. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to the invention commensurate in scope with these claims. .

It is not clear that the claimed method would be suitable for the recovery of any and all bacteria. From the record of the written disclosure specific bacteria were obtained by the cultivation of the specific cell lines in specific media. In view of the specific nutritional requirements of different types of "cell cultures" and of different bacteria, there is no reasonable expectation that any and all types of bacteria may be "produced" or even isolated from any and all cell cultures by the procedure claimed. For example, any anaerobic bacteria would be destroyed upon exposure to aerobic conditions. In addition, the claims lack specific method steps for the recovery of the bacteria. Thus, it is unclear that the claimed method would be

suitable for the recovery of any and all bacteria, a few of which may be present, but not detectable by certain means.

Moreover, one of ordinary skill in the art would not reasonably expect any and all possible viral infected eukaryotic cell cultures to harbor or to be contaminated by bacteria, especially if stringent aseptic technique is used. In this respect, it is apparent that only very specific sources of cell cultures would be suitable for the claimed invention. However, the specification provides insufficient guidance for one skilled in the art to obtain such cell cultures.

In addition, it is unclear what precautions were taken in the instant case to assure that the bacteria harvested are not incidental contaminants inadvertently introduced into the cell culture. Moreover, it is well known in the art that the strains of bacteria which were recovered after the claimed method are common cell culture contaminants. Thus, there is no clear correlation between the instant method of culturing and the production of new strains of bacteria.

It is also apparent that the claimed method is unpredictable and would appear to depend on the type of cell cultured and the type of virus employed. It is unclear how the cell culture is chosen to have a reasonable a degree of certainty that bacteria as required can be "produced", in the absence of positive steps to modify existing bacteria and to assure the survival of the cell culture for a time period. What step actually produces the bacterium? Is it sufficient for any bacterium to be grown in any virally-infected eukaryotic cell in order to acquire both eukaryotic and viral genes? Accordingly, in view of the lack of guidance, the claims as written constitute nothing more than an invitation to experiment.

The present invention would also require undue experimentation to practice in view of the unpredictable completion of the culturing steps. The specification indicates that the cultured cells under anaerobic conditions results in the death of the eukaryotic cells. However, the claims include no such

limitation, accordingly, it is unclear if the eukaryotic cells are to be living or dead at this point. Likewise, the specification indicates that culturing under low oxygen conditions results in the production of the bacterium. However, what actual step leads to the production of the bacterium? Where are the genetic elements necessary for this event to occur (i.e., what is the origin of the bacteria)? While it is true that bacteria are a frequent contaminant of a cell culture, it is not apparent that the purpose of the present invention is to recover contaminants. Furthermore, how long is one of skill in the art to culture the virally-infected eukaryotic cells. On the other hand, how long does one of skill in the art have to culture the cells anaerobically in order to "produce" a bacterium containing a eukaryotic and/or viral gene? Likewise, which eukaryotic cells should one use, and what virus should be employed?

Additionally, it is unclear how one of skill in the art would determine and assure that the actual viral and/or eukaryotic genes are indeed intact genes picked up rather than random fragments thereof. The cell line of the specification uses retrovirally-infected cells. However, by convention, retroviral genes have been found to be ubiquitous in all types of different organisms, such that virtually any cell culture would reasonably be expected to have at least pieces of DNA from these viruses. In addition, it is well known in the art that many animals species harbor endogenous retroviral genes. However, it is unclear how one skilled in the art would determine that the cell culture has these "genes" without undue experimentation. Regarding the genes or fragments that are to be present in the bacteria, it is unclear whether such pieces are to be stably incorporated into the genome and that proteins will be expressed by them. For DNA to integrate homologous recombination is needed, such that the respective sequences must already be present in the bacteria. Therefore, it is unclear whether a stable product is produced.

In view of the lack of guidance provided by the disclosure, the limited number of working examples, the state of the art, the breadth of the claims, and the unpredictably nature of the invention, it would take an undue amount of experimentation to practice the claimed invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-25 are 11-12, and 19 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 1 and 15 are rendered vague and indefinite by use of the language "producing" with respect to the bacteria harvested, since it is unclear that "production" occurs. Moreover, it cannot be assessed whether any DNA picked up would necessarily constitute a gene, but rather parts of introns, pseudogenes, "junk DNA", etc..

Claims 1 and 15 are rendered vague and indefinite by the use of the language "under low oxygen conditions...". The metes and bounds of this claim terminology is unclear. What is a low oxygen condition? How low should the oxygen content be?

Claims 2 , 3, and 15 are vague and indefinite and confusing. These claims recite "subjecting the cells to an aerobic culturing step", yet they depend upon claims which require culturing under low oxygen conditions. Accordingly, such claims are contradictory.

Claims 11-12 and 19 recite the limitation "L-cell virus". There is insufficient antecedent basis for this limitation in the claim because the independent claims lack a full spelling of the complete virus name, prior to abbreviation because it does not appear that this a term of the art.

Claims 2 and 15 are vague and indefinite in the use of the language "microaerophilic conditions". What is meant by this term? It does not appear that this is a term of the art.

Claims 1-24 are incomplete in the absence of a recovery step for the microorganisms obtained.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.
>
> (e) the invention was described in a patent granted on an application for patent by another filed in the United States before the invention thereof by the applicant for patent, or on an international application by another who has fulfilled the requirements of paragraphs (1), (2), and (4) of section 371© of this title before the invention thereof by the applicant for patent.

Claim 24 and 25 are rejected under 35 U.S.C. 102(b) as anticipated by or, in the alternative, under 35 U.S.C. 103(a) as obvious over (1) Bujard et al. (U.S. Patent No. 4,868,111, IDS-6) or (2) Sloma et al. (U.S. Patent No. 4,695,543, IDS-6).

The claims are drawn to a bacterium containing a eukaryotic gene prepared by the method of the instant disclosure. This has been broadly interpreted as any bacterium containing any gene coding for eukaryotic peptide.

Bujard et al. and Sloma et al. teach a bacterium containing a eukaryotic gene. For instance, Bujard et al. teaches a bacterial expression system and a process for producing a prokaryotic or eukaryotic polypeptide. More specifically, Bujard et al. teaches a bacterium, *Bacillus subtilis*, which contains the gene coding for mouse dihydrofolate reductase (i.e., a eukaryotic gene) (see claims). Similarly, Sloma et al.

teaches an *Escherichia coli* that has been transformed with a plasmid containing the human alpha-interferon gene (i.e., a bacterium containing a eukaryotic gene).

Thus, claims 24 and 25 constitute a Product-by-Process type claim. In a product-by-process claim, the process of producing the product is given no patentable weight. *In re Brown*, 173 USPQ 685 (CCP 1972). Since the Patent Office does not have the facilities for examining and comparing Applicant's composition with the compositions of the prior art references, the burden is upon Applicants to show a distinction between the material, structural, and functional characteristics of the claimed composition and the compositions of the prior art. See In re Best, 562 F.2d 1252, 195 U.S.P.Q. 430 (CCPA 1977).

Conclusion

No claims allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A. Zeman whose telephone number is (703) 308-7991. The examiner can be reached between the hours of 7:30 am and 4:00 pm Monday through Friday.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner can be reached at (703) 308-1032 or the examiner's supervisor, Lynette Smith, can be reached at (703)308-3909.

Robert A. Zeman

July 13, 2000

DONNA WORTMAN
PRIMARY EXAMINER